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CASE REPORT

Paradoxical worsening of pulmonary *Mycobacterium abscessus*

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Summary
Transient worsening of tuberculosis (TB) symptomatology and lesions in response to anti-TB therapy has previously been reported as paradoxical worsening. Recently, paradoxical worsening of TB following antiretroviral therapy in AIDS patients was reported. However, paradoxical worsening of nontuberculous mycobacterium, including *Mycobacterium abscessus* (*M. abscessus*), has not been reported previously. We reported the first case of paradoxical worsening of pulmonary *M. abscessus*.

Case report

A 73-year-old woman with persistent productive cough and high grade fever of 38 °C presented at our hospital on 30 May, 2005. She was referred by a local doctor for suspicion of pulmonary tuberculosis (TB) due to abnormal shadow on chest radiograph. The patient had been well until 2 months earlier, when she complained of a cough producting yellowish-to-dark-gray sputum and low grade fever. There was no history of allergy, previous major illness, or risk factors for immunodeficiency. On admission, the white-cell count was 8800 per cubic millimeter, with 72 percent neutrophils, 14 percent lymphocytes, 8 percent monocytes, 1 percent eosinophils. The lymphocyte count was 1687 per cubic millimeter. Serum C-reactive protein showed an elevation to 3.99 mg/dl (normal range <0.3 mg/dl). The value for liver and renal functions were normal and serum fasting glucose level was normal. A tuberculin skin test (purified protein derivative, 5 TU) was positive. Plain chest radiograph demonstrated consolidation with infiltration in the left lingula and slight infiltration in the left S^{1+2} (Fig. 1(a)). Chest computed tomography showed air space consolidation in the left lingula with surrounding ground glass opacity and small centrilobular opacity in the left S^{1+2} (Fig. 2(a)). Sputum smear and culture yielded acid-fast bacilli and *Mycobacterium abscessus* was detected by fluoromatric deoxyribonucleic acid deoxyribonucleic acid hybridization

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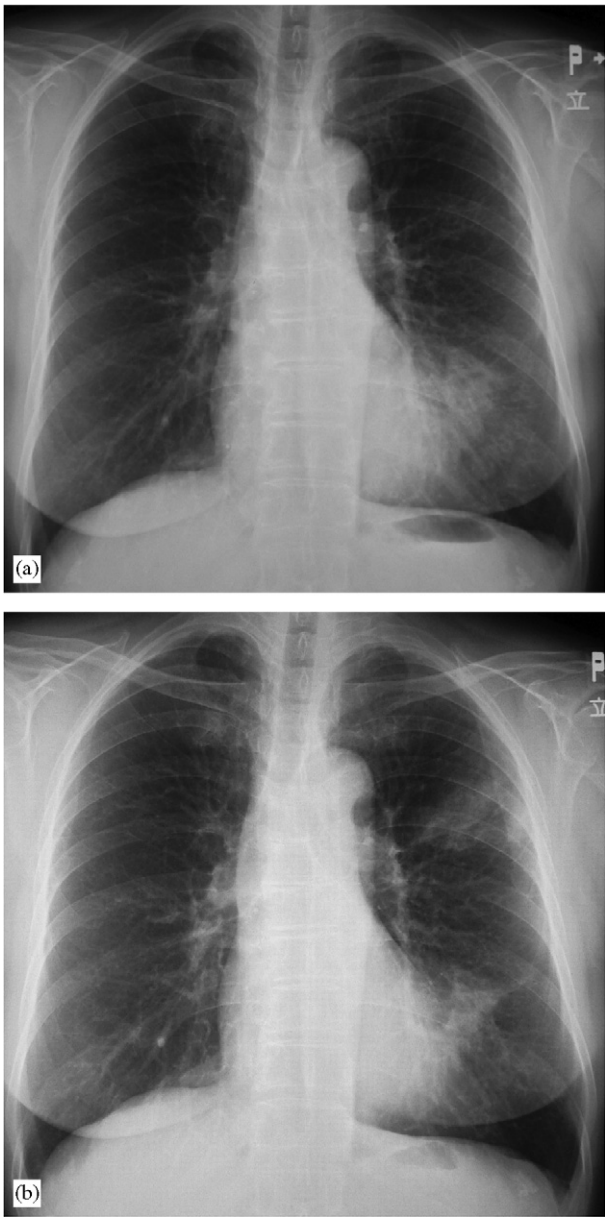

Figure 1 (a) Chest radiograph on admission. (b) Chest radiograph 2 weeks after medical treatment.

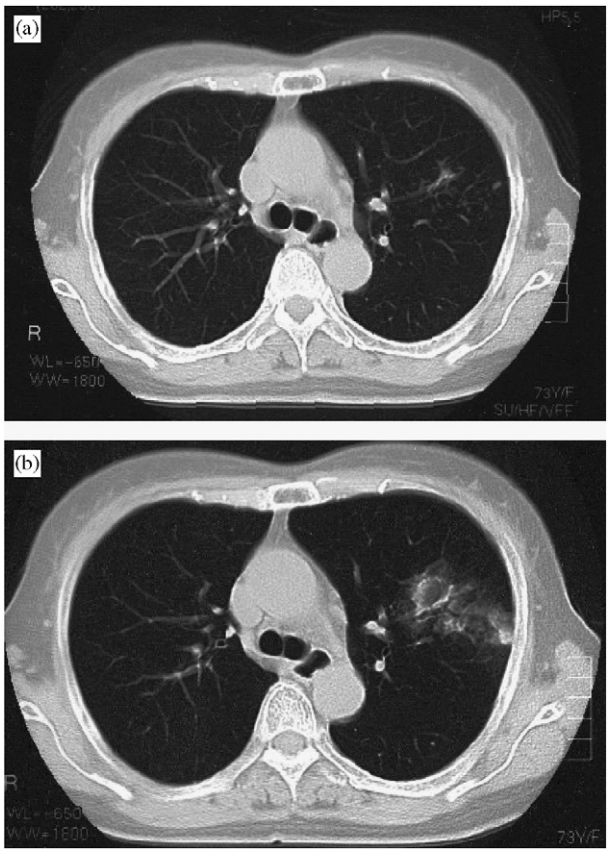

Figure 2 (a) CT scan of the thorax on admission. (b) CT scan of the thorax showing paradoxical worsening.

Table 1 Susceptibility test for bacteria minimum inhibitory concentration (MIC).

Drug	MIC (μg/ml)
Imipenem	<0.5
Minomycin	<1
Amikacin	<2
Isepacin	<2

(DDH mycobacteria, Kyokuto co., Ltd.). Anti-TB drugs containing rifampicin (450 mg/day), isoniazide (300 mg/day), ethambutol (750 mg/day) and pyrazinamide (1.2 g/day) were administrated from 30 May, 2005. After identification of *M. abscessus*, the drugs were changed to meropenem (1 g/day) and amikacin (200 mg/day) intravenously and oral clarithromycin (400 mg/day) from 15 June. Susceptibility test showed resistance to all anti-TB drugs. And the dilution antimicrobial susceptibility test for bacteria (MicroScan®, Dade Behring co., Ltd., Tokyo) was performed. The minimal inhibitory concentration (MIC) for drugs are shown in a list (Table 1). Two weeks after these medical treatment, the chest radiograph showed a new lesion in the left upper lobe (Figs. 1(b) and 2(b)). The white-cell count was 8400 per cubic millimeter, with 58 percent neutrophils, 33 percent lymphocytes, 6 percent monocytes, 2 percent eosinophils and 1 percent basophils. The lymphocyte count increased to 2772 per cubic millimeter. As she did not complain of any symptoms, based on a diagnosis of paradoxical worsening of *M. abscessus*, the treatment was continued. However, left upper lobe opacity did not change, although the lingual opacity improved slightly. Therefore, we performed bronchoscopic examination on 22 July, which demonstrated yellowish gray mucus throughout the left bronchial tree. Microscopic examination of a transbronchial biopsy specimen disclosed noncaseating small granuloma with chronic inflammation and these findings were compatible with pulmonary *M. abscessus* lesion. Microscopical examination of bronchial washing specimen was negative; the culture did not yield any pathogens. We continued the same medical treatment with

clarithromycin and minomycin and the patient was discharged on 29 July. Opacity in the left S^{1+2} and the lingula had almost disappeared by September 2005. The white-cell count was 5600 per cubic millimeter, with 52 percent neutrophils, 36 percent lymphocytes, 6 percent monocytes, 5 percent eosinophils and 1 percent basophils. The lymphocytes count decreased to 2016 per cubic millimeter. To date, we have followed the patient in our outpatient clinic for 8 months without regression.

Discussion

We reported a case showing paradoxical worsening of pulmonary *M. abscessus*. It is generally considered that the immune restoration syndrome represents an immune reaction to antigens released by treated TB. Paradoxical worsening of signs and symptoms of TB may occur when HIV-infected patients are treated effectively for TB and have commenced HAART.[1–3] The incidence of paradoxical worsening reactions is probably related to the reconstitution of T-cell proliferation and function leading to increased interferon-γ secretion after initiation of HARRT.[4]

While sputum smear was positive at admission, the smear and culture of bronchial washing specimen was negative at paradoxical worsening. And the histology of transbronchial biopsy specimen from the left upper lesion at paradoxical worsening was compatible with *M. abscessus* lesion and continued therapy with clarythromicin and minomycin ultimately resulted in radiological improvement. The lymphocyte count increased from 1681 to 2772 after the beginning of treatment. The increase in lymphocytes after treatment might reflect immune restoration.

In summary, we reported the first case of paradoxical worsening involving *M. abscessus* infection. Effective drugs might improve the immune reaction following paradoxical worsening with recovery of the lymphocyte count. We must consider the potential for paradoxical worsening in *M. abscessus* despite the administration of effective drugs.

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